Workshop on Inhibitors to Factor VIII

November 21, 2003

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Issues

Inhibitor formation to factor VIII is the chief adverse event associated with the use of antihemophilic products

How can we ensure that new factor VIII products, or products that have undergone significant manufacturing changes won't induce inhibitor formation in previously treated patients?

To what extent is immunogenicity a property of the product, rather than the patient?

Workshop Objectives

- Improve clinical trial design
- Review available data on the prevalence and incidence of inhibitor formation
- Examine the limitations and potentials of assays for factor VIII inhibitors
- Increase international harmonization
- Explore future directions and collaborative studies

Scientific and Regulatory Agenda

- Overview of factor VIII inhibitors
- Environmental and genetic factors that may influence inhibitor antibody formation
- What pre-clinical testing of factor VIII concentrates can tell us: A cautionary tale

<u>Inhibitor assay</u>

- Regulatory aspects of the factor VIII inhibitor assay
- Innovations in the factor VIII inhibitor assay

Scientific and Regulatory Agenda

- ISTH rationale of recommendations for use of previously treated patients (PTPs) in clinical trials

Inhibitor surveys

- Canadian experience with factor VIII inhibitors during conversion to recombinant products
- Occurrence of inhibitors among patients enrolled in the U.S. Hemophilia Universal Data Collection project

Scientific and Regulatory Agenda

Regulatory Considerations

- Requirements of the EMEA
- FDA recommendations for clinical trials
- Statistical considerations for design of FDA clinical trials
- Role of the data safety monitoring board in clinical trials

Scientific and Regulatory Agenda

Industry Perspectives

Baxter

Bayer

Biomeasure/Octagen

Wyeth

Future Directions

- Preliminary ideas on prospective international studies of product-related factor VIII inhibitor formation
- Panel Discussion